

2. The non-technical abstract

We propose to administer a therapeutic vaccine to 24 patients with recurrent advanced carcinoma of the oral cavity or oropharynx who are HLA-A2+ and capable of responding to at least one common skin test antigen. These two requirements are necessary for the patients to make an immune response to the vaccine. The vaccine will consist of irradiated “master cells” into which DNA (nucleic acid) obtained from the patient’s own tumor will be introduced by co-incubation of the cells with the DNA-lipid mixture. The “master cells” are an HLA-A2+ squamous cell carcinoma of the head and neck (SCCHN) cell line maintained in culture in the investigators’ laboratory and previously modified by a retroviral transfer of the human IL-2 gene to secrete IL-2 (a growth factor for immune cells). A bank of “master cells” will be prepared and tested for safety and sterility prior to its use for DNA transfer to make individual vaccines. The objectives are: 1) to evaluate safety of the vaccine for the patients and 2) to determine if the DNA-based vaccine induces an immune response to the tumor. In order to evaluate safety, the vaccine will be administered to groups of patients in such a way that the first group will receive the lowest number of irradiated vaccine cells, and only in the absence of grade 3 or 4 toxicity, the second group of patients will receive the intermediate dose of the vaccine. The third group of patients will be vaccinated with the highest dose of the vaccine provided no grade 3 or 4 toxicity is observed in the previous group of patients, who received the intermediate vaccine dose. To evaluate immunologic responses to the tumor, specific assays will be performed prior to, during and after vaccination for the presence and frequency in the peripheral blood of T lymphocytes capable of responding to each patient’s own tumor. This DNA-based vaccination strategy combines several of the known requirements for successful vaccination, namely, the presentation by the “master cell” of tumor antigens specified by the tumor-derived DNA, shared tumor antigens (this cell is a tumor of the same type as the patient’s own tumor) and foreign HLA antigens (this cell is only matched for HLA-A2 with the patient) as well as the ability to secrete IL-2, which is necessary for generation of immune responses. It is expected that this vaccine will be safe and capable of eliciting robust anti-tumor immune responses in patients with advanced oral carcinoma.